Am J Transl Res 2025;17(4):3142-3151
www.ajtr.org /ISSN:1943-8141/AJTR0163129

Original Article

Montelukast sodium combined with levocabastine nasal spray demonstrates high efficacy in treating pediatric allergic rhinitis

Jing Yang[1], Yaping Wang[2], Linglong Li[3], Juan Xiong[3], Dehong Mao[3]

[1]School of Clinical Medicine, Chengdu University of Traditional Chinese Medicine, Chengdu 610075, Sichuan, China; [2]College of Integrated Traditional Chinese and Western Medicine, Chongqing Medical University, Chongqing 400016, China; [3]Department of Otolaryngology, Yongchuan Hospital of Traditional Chinese Medicine, Chengdu University of Traditional Chinese Medicine, Chongqing 402160, China

Received January 6, 2025; Accepted March 17, 2025; Epub April 15, 2025; Published April 30, 2025

Abstract: Objectives: To investigate the efficacy and safety of montelukast sodium (MKS) combined with levocabastine (LEVO) nasal spray in treating pediatric allergic rhinitis and its impact on quality of life (AR). Methods: A total of 125 pediatric AR patients, diagnosed between September 2022 and September 2024, were enrolled and divided into two groups. The research group (n = 65) received MKS plus LEVO nasal spray, while the control group (n = 60) received LEVO nasal spray alone. Treatment efficacy, safety (assessing xerostomia, headache, and gastrointestinal disturbances), and clinical symptom scores (rhinorrhea, sneezing, nasal obstruction, and nasal pruritus) were evaluated. Additionally, nasal cavity parameters (nasal resistance (NR), minimum cross-sectional area (mCSA), and nasal cavity volume (NCV)), serum inflammatory markers (IL-4, IL-8, IL-10), serum biochemical indices (total immunoglobulin E [TIgE], eosinophil count [EOS], eosinophil cationic protein [ECP]), and quality of life (Rhinoconjunctivitis Quality of Life Questionnaire [RQLQ]) were analyzed. Univariate and multivariate binary logistic regression analyses were conducted to identify factors influencing treatment outcomes. Results: The research group demonstrated significantly higher overall treatment efficacy than the control group ($P<0.05$), with a comparable safety profile ($P>0.05$). Post-treatment, clinical symptom scores, IL-4, IL-8, TIgE, EOS, ECP levels and RQLQ scores were significantly reduced in the research group compared to the control group (all $P<0.05$). Conversely, IL-10 levels were significantly higher in the research group (both $P<0.05$). Notably, passive secondhand smoke exposure, IL-10, EOS, and treatment modality were significantly associated with treatment efficacy (all $P<0.05$). Binary logistic regression identified passive secondhand smoke exposure ($P = 0.035$) and EOS ($P = 0.036$) as independent risk factors for treatment outcomes. Conclusions: The combination of MKS and LEVO nasal spray demonstrates superior efficacy and safety in pediatric AR treatment, significantly improving patients' quality of life. Moreover, treatment failure is closely linked to passive secondhand smoke exposure and elevated EOS levels.

Keywords: Montelukast sodium, levocabastine nasal spray, pediatric allergic rhinitis, efficacy, safety, quality of life

Introduction

Allergic rhinitis (AR) is a common, non-infectious, chronic inflammatory disorder of the nasal mucosa, characterized by symptoms such as rhinorrhea, sneezing, nasal congestion, and nasal pruritus [1, 2]. Epidemiological data suggest that AR negatively affects approximately 10.0% to 40.0% of children worldwide, with a lifetime risk of around 20.0%. Notably, its incidence has been rising significantly in recent years [3, 4]. The pathogenesis of AR is primarily linked to an immunoglobulin E (IgE)-mediated response triggered by allergen exposure. These allergens include house dust mites, fungi, pet dander, indoor plants, and grass pollens [5]. While allergen avoidance remains the primary preventive strategy, it is often impractical in real-world settings [6].

Pharmacological therapy is the cornerstone of AR management. Available treatments include antihistamines, leukotriene receptor antagonists, mast cell stabilizers, corticosteroids, and

https://doi.org/10.62347/HYBG4442

decongestants [7]. However, no single medication has been proven to completely cure AR in children [8]. This highlights the need to explore effective therapeutic approaches to improve treatment efficacy and enhance the quality of life in pediatric AR patients.

Levocabastine (LEVO) nasal spray, an intranasal antihistamine, acts by inhibiting key mediators involved in nasal mucosal allergic inflammation [9]. It provides rapid symptom relief, often within 30 minutes of administration, but symptom recurrence remains a concern [10]. Montelukast sodium (MKS), a leukotriene receptor antagonist, suppresses leukotriene-mediated inflammation by blocking receptor binding, thereby exerting anti-inflammatory and anti-asthmatic effects [11]. Previous studies have explored the combination of MKS with various agents for AR management [12, 13]. For instance, Shao et al. [14] indicated that montelukast combined with levocetirizine effectively alleviated AR symptoms while maintaining a favorable safety profile in patients with AR and asthma syndrome.

This study aims to evaluate the efficacy and safety of the combined use of LEVO nasal spray and MKS in pediatric AR treatment. Despite the potential benefits of this combination, relevant research remains limited. By addressing this gap, our study provides new insights into optimizing treatment strategies for pediatric AR, underscoring its clinical significance and innovative approach.

Materials and methods

Patient selection

This retrospective study enrolled 125 pediatric patients diagnosed with AR between September 2022 and September 2024. The research group (n = 65) received a combination of MKS and LEVO nasal spray, while the control group (n = 60) was treated with LEVO nasal spray alone. This study was approved by the Institutional Ethics Committee of Yongchuan Hospital of Traditional Chinese Medicine, Chengdu University of Traditional Chinese Medicine.

Inclusion criteria: (1) Patients met the diagnostic criteria for pediatric AR as per established guidelines [15]. (2) Patients had not received any anti-allergic medications recently. (3) Patients were between 2 and 14 years of age. (4) Patients had not been treated with leukotriene receptor antagonists or antihistamines in the past three months. (5) Patients had complete medical records available for review.

Exclusion criteria: Patients were excluded if they had: (1) Severe nasal polyps, nasal septum deviation, or chronic sinusitis. (2) Frequent and severe bronchial asthma exacerbations in the past month or concomitant severe chronic respiratory diseases. (3) A history of nasal surgery. (4) Underlying autoimmune or endocrine disorders. (5) Known allergies to the study medications.

Patient selection was conducted through a systematic search of the hospital's medical records. The flowchart illustrating patient inclusion and exclusion criteria is presented in **Figure 1**.

Treatment protocols

The control group was treated with LEVO nasal spray, administered as follows: two sprays per nostril, twice daily. Patients were advised to clear their nasal passages before each administration.

The research group received a combination therapy consisting of LEVO nasal spray (administered identically to the control group) and oral MKS. MKS was administered as one tablet, once daily. Both groups underwent continuous treatment for four weeks.

Data extraction and validation

Relevant data were retrieved from the hospital's medical record system. A comprehensive comparative analysis was conducted between the two groups based on multiple parameters, including treatment efficacy, safety (incidence of dry mouth, headache, and gastrointestinal reactions), clinical symptom scores (rhinorrhea, sneezing, nasal congestion, and nasal pruritus), nasal cavity condition (nasal resistance [NR], minimum cross-sectional area [mCSA], and nasal cavity volume [NCV]), serum inflammatory markers (interleukin [IL]-4, IL-8, IL-10), serum biochemical indices (total immunoglobulin E [tIgE], eosinophil count [EOS], and eosinophil cationic protein [ECP]), and quality of

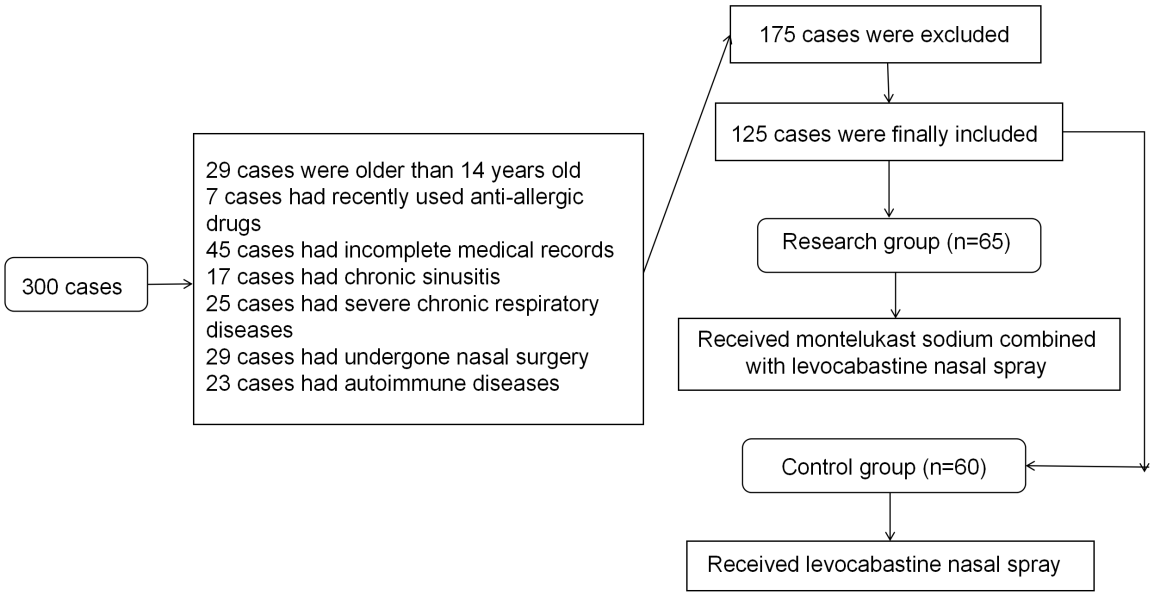

Figure 1. Research flowchart.

life (assessed via the Rhinoconjunctivitis Quality of Life Questionnaire [RQLQ]). All extracted data were subsequently validated for accuracy.

(1) Treatment efficacy: Treatment efficacy was assessed based on the following criteria: Cured: Complete resolution of inflammation with disappearance of sneezing, rhinorrhea, nasal congestion, and nasal pruritus. Significantly effective: Substantial improvement in symptoms with controlled inflammation. Effective: Partial improvement in rhinitis symptoms, although inflammation persisted. Ineffective: No improvement or worsening of symptoms. The total effective rate was calculated as the proportion of patients classified as cured, significantly effective, or effective relative to the total number of patients.

(2) Safety: Adverse reactions, including dry mouth, headache, and gastrointestinal symptoms, were closely monitored in both groups. The incidence rates of these adverse events were documented and analyzed.

(3) Clinical symptom scoring: Nasal symptoms were assessed using a rhinitis symptom score scale before treatment and four weeks after treatment. The scale assigned scores as follows: 0: Normal; 1: Mild symptoms; 2: Moderate symptoms; 3: Severe symptoms.

(4) Nasal cavity condition: Nasal cavity parameters were measured using acoustic rhinometry to assess nasal resistance, minimum cross-sectional area, and nasal cavity volume. Prior to measurement, patients were seated in a relaxed position for 15 minutes. The probe was then carefully inserted into the nostril while the patient held their breath, ensuring accurate measurements. Assessments were conducted at baseline and four weeks post-treatment.

(5) Inflammatory markers: Five milliliters of fasting venous blood were collected from each patient before treatment and two weeks after treatment. Following centrifugation, serum samples were analyzed for IL-4, IL-8, and IL-10 levels using enzyme-linked immunosorbent assay (ELISA).

(6) Serum biochemical indices: tIgE levels were measured using ELISA. Serum EOS count was determined using an automated biochemical analyzer. Serum ECP levels were assessed via spectrophotometric colorimetry. All measurements were performed at baseline and two weeks after treatment.

(7) Quality of life: The RQLQ [16] was used to evaluate quality of life before treatment and four weeks post-treatment. The questionnaire comprises 28 items scored on a 0-6 scale: 0: No impact; 1: Almost no impact; 2: Slight

Table 1. Comparative analysis of general characteristics

Indicators	Research group (n = 65)	Control group (n = 60)	χ^2/t	P
Sex			0.017	0.897
Male	35 (53.85)	33 (55.00)		
Female	30 (46.15)	27 (45.00)		
Age (years)	7.63±1.97	7.57±1.70	0.182	0.856
Disease course (years)	15.17±3.64	15.55±4.66	0.510	0.611
Bronchial asthma			0.069	0.792
Without	53 (81.54)	50 (83.33)		
With	12 (18.46)	10 (16.67)		
Passive secondhand smoke exposure			1.039	0.308
No	32 (49.23)	35 (58.33)		
Yes	33 (50.77)	25 (41.67)		

Table 2. Comparative analysis of efficacy

Indicators	Research group (n = 65)	Control group (n = 60)	χ^2	P
Cured	33 (50.77)	18 (30.00)		
Significantly effective	17 (26.15)	24 (40.00)		
Effective	10 (15.38)	6 (10.00)		
Ineffective	5 (7.69)	12 (20.00)		
Total effective rate	60 (92.31)	48 (80.00)	4.022	0.045

impact; 3: Mild impact; 4: Moderate impact; 5: Severe impact; 6: Extremely severe impact; Lower scores indicate a better quality of life.

Among these indicators, the primary outcome measures were treatment efficacy, safety, clinical symptom scores, and quality of life, while secondary outcome measures included nasal cavity condition, inflammatory markers, and serum biochemical indices.

Statistical analysis

Categorical variables were presented as frequencies and percentages (n/%). Continuous variables were expressed as mean ± standard error of the mean (SEM).

Comparisons of categorical data between groups were performed using the chi-square (χ^2) test. Comparisons of continuous variables between independent groups were conducted using the independent-sample t-test. Within-group changes before and after treatment were analyzed using the paired t-test. All statistical analyses were performed using SPSS 24.0. A *P*-value <0.05 was considered statistically significant.

Results

Comparative analysis of general characteristics

No significant differences were observed between the research and control groups in terms of gender, age, disease duration, coexisting bronchial asthma, and passive secondhand smoke exposure (all P>0.05) (**Table 1**).

Comparative analysis of treatment efficacy

The total effective rate in the research group was 92.31%, significantly higher than 80.00% in the control group (P<0.05) (**Table 2**).

Comparative analysis of safety

The total incidence of adverse reactions, including dry mouth, headache, and gastrointestinal symptoms, was 7.69% in the research group, comparable to 6.67% in the control group (P>0.05) (**Table 3**).

Comparative analysis of clinical symptom scores

Before treatment, clinical symptom scores for rhinorrhea, sneezing, nasal congestion, and nasal pruritus showed no significant differences between the two groups (P>0.05). After treatment, both groups exhibited a significant reduction in symptom scores (P<0.05), with

Table 3. Comparative analysis of safety

Indicators	Research group (n = 65)	Control group (n = 60)	χ^2	P
Dry mouth	1 (1.54)	1 (1.67)		
Headache	2 (3.08)	1 (1.67)		
Gastrointestinal reactions	2 (3.08)	2 (3.33)		
Total	5 (7.69)	4 (6.67)	0.049	0.825

Table 4. Comparative analysis of clinical symptom scores

Indicators	Research group (n = 65)	Control group (n = 60)	t	P
Rhinorrhea				
Before	2.51±0.53	2.38±0.56	1.333	0.185
After	0.97±0.39[b]	1.93±0.63[a]	10.329	<0.001
Sneezing				
Before	2.37±0.52	2.28±0.56	0.932	0.353
After	0.75±0.43[b]	1.42±0.50[a]	8.050	<0.001
Nasal congestion				
Before	2.68±0.47	2.60±0.49	0.932	0.353
After	0.80±0.40[b]	1.28±0.61[a]	5.241	<0.001
Nasal pruritus				
Before	2.51±0.50	2.52±0.50	0.112	0.911
After	0.83±0.38[b]	1.40±0.56[a]	6.704	<0.001

Note: [a]P<0.05, [b]P<0.01 *vs.* before treatment.

the research group showing significantly lower scores than the control group (P<0.05) (**Table 4**).

Comparative analysis of nasal cavity condition

Baseline measurements of nasal cavity condition resistance (NR), minimum cross-sectional area (mCSA), and nasal cavity volume (NCV) showed no significant differences between groups (P>0.05). Following treatment, both groups exhibited a significant reduction in NR and mCSA and a significant increase in NCV (P<0.05). Notably, the research group showed significantly lower NR and mCSA and higher NCV compared to the control group (P<0.05) (**Table 5**).

Comparative analysis of serum inflammatory markers

Before treatment, no significant differences were found in IL-4, IL-8, and IL-10 levels between the groups (all P>0.05). Post-treatment analysis revealed a significant reduction in IL-4 and IL-8 levels and a significant increase in IL-10 levels in both groups (all P<0.05). Moreover, IL-4 and IL-8 levels in the research group were significantly lower, while IL-10 levels were significantly higher than those in the control group (all P<0.05). See **Figure 2**.

Comparative analysis of serum biochemical indices

At baseline, tIgE, EOS, and ECP levels were similar between the groups (all P>0.05). After treatment, all three parameters were significantly reduced in both groups (all P<0.05), with tIgE, EOS, and ECP levels in the research group significantly lower than those in the control group (all P<0.05). See **Figure 3**.

Comparative analysis of quality of life

Prior to treatment, RQLQ scores were comparable between the two groups (P>0.05). After treatment, a significant decrease in RQLQ scores was observed in both groups (P<0.05), with the research group achieving a significantly lower RQLQ score compared to the control group (P<0.05). See **Table 6**.

Univariate and multivariate analyses of factors influencing treatment efficacy

Univariate analysis identified passive secondhand smoke exposure, IL-10 levels, EOS count, and treatment modality as significant factors associated with treatment efficacy (P<0.05). These variables were incorporated as independent factors in a binary logistic regression model, with treatment efficacy (effective/ineffective) as the dependent variable.

Multivariate analysis confirmed that passive secondhand smoke exposure (P = 0.035) and elevated EOS (P = 0.036) were independent risk factors negatively affecting treatment efficacy in pediatric AR (**Tables 7-9**).

Table 5. Comparative analysis of nasal cavity metrics

Indicators	Research group (n = 65)	Control group (n = 60)	t	P
Nasal resistance (cm^3)				
Before	3.34±0.51	3.20±0.42	1.667	0.098
After	2.55±0.38[b]	2.95±0.33[a]	6.260	<0.001
Minimum crosssectional area (cm^2)				
Before	0.69±0.19	0.77±0.28	1.882	0.062
After	0.39±0.10[b]	0.57±0.16[a]	7.604	<0.001
Nasal cavity volume ($cmH_2O/L/min$)				
Before	2.03±0.38	2.10±0.42	0.978	0.330
After	2.80±0.42[b]	2.48±0.38[a]	4.454	<0.001

Note: [a]P<0.05, [b]P<0.01 *vs.* before treatment.

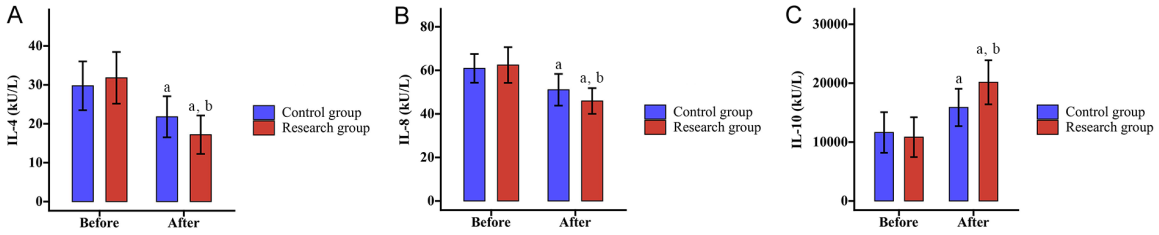

Figure 2. Comparative analysis of serum inflammatory markers between the two groups. A. Pre- and post-treatment IL-4 levels in both groups. B. Pre- and post-treatment IL-8 in the two groups. C. Pre- and post-treatment IL-10 in the two groups. Note: [a]P<0.05 *vs.* before treatment; [b]P<0.05 *vs.* Control. IL, including interleukin.

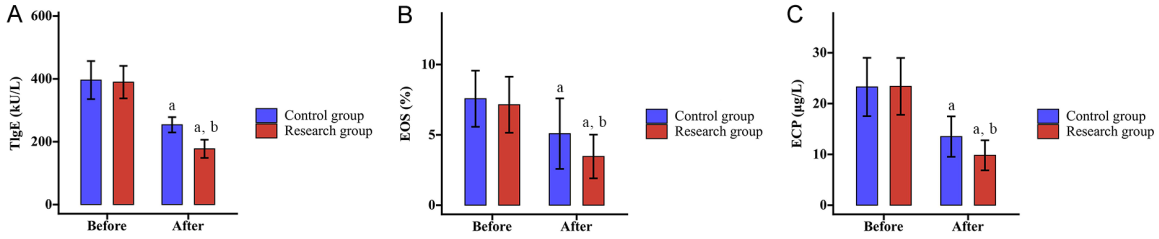

Figure 3. Comparative analysis of serum biochemical indices between the two groups. A. Pre- and post-treatment TIgE in the two groups. B. Pre- and post-treatment EOS in the two groups. C. Pre- and post-treatment ECP in the two groups. Note: [a]P<0.05 *vs.* before treatment; [b]P<0.05 *vs.* Control. TIgE, total immunoglobulin E; EOS, eosinophil count; ECP, eosinophil cationic protein.

Table 6. Comparative analysis of quality of life

Indicators	Research group (n = 65)	Control group (n = 60)	t	P
Before	24.60±3.55	24.30±3.93	0.448	0.655
After	7.86±2.49[b]	12.95±3.47[a]	9.476	<0.001

Note: [a]P<0.05, [b]P<0.01 *vs.* before treatment.

Discussion

AR is an inflammatory disorder of the nasal mucosa characterized by various allergic symptoms. It not only increases the risk of comorbid conditions such as asthma, sinusitis, and conjunctivitis but also negatively impacts patients' social activities, academic performance, and overall quality of life [15, 17]. Given these implications, optimizing treatment strategies to enhance symptom control and therapeutic efficacy in pediatric AR remains a clinical priority.

The findings of this study demonstrated that the combination therapy of MKS and LEVO

Table 7. Univariate analysis of factors influencing treatment efficacy

Indicators	Ineffective group (n = 17)	Effective group (n = 108)	χ^2/t	P
Gender			0.155	0.694
Male (n = 68)	10 (58.82)	58 (53.70)		
Female (n = 57)	7 (41.18)	50 (46.30)		
Age (years)			0.638	0.424
<8 (n = 55)	9 (52.94)	46 (42.59)		
≥8 (n = 70)	8 (47.06)	62 (57.41)		
Disease course (years)			2.895	0.089
<15 (n = 57)	11 (64.71)	46 (42.59)		
≥15 (n = 68)	6 (35.29)	62 (57.41)		
Bronchial asthma			1.893	0.169
Without (n = 103)	12 (70.59)	91 (84.26)		
With (n = 22)	5 (29.41)	17 (15.74)		
Passive secondhand smoke exposure			4.629	0.031
No (n = 67)	5 (29.41)	62 (57.41)		
Yes (n = 58)	12 (70.59)	46 (42.59)		
IL-4 (kU/L)			0.408	0.523
<30 (n = 50)	8 (47.06)	42 (38.89)		
≥30 (n = 75)	9 (52.94)	66 (61.11)		
IL-8 (kU/L)			1.373	0.241
<60 (n = 50)	9 (52.94)	41 (37.96)		
≥60 (n = 75)	8 (47.06)	67 (62.04)		
IL-10 (kU/L)			4.720	0.030
<11000 (n = 65)	13 (76.47)	52 (48.15)		
≥11000 (n = 60)	4 (23.53)	56 (51.85)		
TIgE (kU/L)			0.033	0.856
<400 (n = 71)	10 (58.82)	61 (56.48)		
≥400 (n = 54)	7 (41.18)	47 (43.52)		
EOS (%)			4.324	0.038
<7.50 (n = 73)	6 (35.29)	67 (62.04)		
≥7.50 (n = 52)	11 (64.71)	41 (37.96)		
ECP (μg/L)			0.506	0.477
<24 (n = 42)	7 (41.18)	35 (32.41)		
≥24 (n = 83)	10 (58.82)	73 (67.59)		
Treatment modality			4.022	0.045
Levocabastine nasal spray (n = 60)	12 (70.59)	48 (44.44)		
Montelukast sodium plus levocabastine nasal spray (n = 65)	5 (29.41)	60 (55.56)		

Note: IL, interleukin; TIgE, total immunoglobulin E; EOS, eosinophil count; ECP, eosinophil cationic protein.

nasal spray achieved a significantly higher overall treatment efficacy rate than LEVO monotherapy (92.31% vs. 80.00%). Consistent with research by Yao et al. [18], the therapeutic efficacy of MKS in pediatric AR may be partially influenced by the G473A polymorphism of the lysyl oxidase (LOX) gene, which could account for the superior outcomes observed with MKS-based treatment.

Furthermore, the combined MKS and LEVO regimen exhibited a favorable safety profile, with an incidence of adverse reactions comparable to that of LEVO monotherapy (7.69% vs. 6.67%). MKS has been well-documented as a safe and well-tolerated treatment in pediatric AR, with no reported cardiotoxic effects, which may contribute to the safety of this combination therapy [19].

Table 8. Variable assignment analysis of significant factors identified in univariate analysis

Indicators	Variable	Assignment
Passive secondhand smoke exposure	X1	No = 0, yes = 1
IL-10 (kU/L)	X2	<11000 = 0, ≥11000 = 1
EOS (%)	X3	<7.50 = 0, ≥7.50 = 1
Treatment modality	X4	Montelukast sodium plus levocabastine nasal spray = 0, levocabastine nasal spray = 1
Efficacy	Y	Effective = 0, ineffective = 1

Note: IL, interleukin; EOS, eosinophil count.

Table 9. Multivariate analysis of factors influencing treatment efficacy using binary logistic regression model

Factors	β	SE	Wald	P	OR	95% CI
Passive secondhand smoke exposure	1.281	0.608	4.449	0.035	3.602	1.095-11.848
IL-10 (kU/L)	-1.129	0.631	3.197	0.074	0.324	0.094-1.115
EOS (%)	1.243	0.594	4.384	0.036	3.467	1.083-11.100
Treatment modality	1.132	0.607	3.476	0.062	3.102	0.944-10.198

Note: IL, interleukin; EOS, eosinophil count.

In addition to its efficacy and safety, the combination therapy significantly improved clinical symptoms (rhinorrhea, sneezing, nasal congestion, and nasal pruritus) and nasal cavity parameters. Similar findings were reported by Micheletto et al. [20], where MKS administration in aspirin-induced asthma patients led to significant improvements in nasal function, supporting the results of the present study.

The pathophysiology of AR involves chronic inflammatory stimulation of the nasal mucosa, which increases permeability and induces tissue damage, exacerbating symptoms [21]. Key inflammatory cytokines, including IL-4, IL-8, and IL-10, play crucial roles in allergic responses. IL-4 and IL-8, as pro-inflammatory cytokines, stimulate IgE production and promote lymphocyte proliferation, thereby aggravating rhinitis symptoms. In contrast, IL-10 is involved in regulating allergic inflammation and immune responses, influencing the disease's progression [22-24].

Furthermore, tIgE, EOS, and ECP play crucial roles in the pathophysiological processes of AR. Specifically, tIgE reflects immunoglobulin activity in patients, EOS contributes to mucosal mucus secretion and serves as an indicator of disease severity, while ECP is closely associated with the onset and progression of AR [25-28]. Based on these pathophysiological mechanisms, our study evaluated these biomarkers in pediatric patients.

Our findings demonstrated that the combination therapy of MKS and LEVO nasal spray was significantly more effective in modulating serum inflammatory markers and inhibiting disease progression in pediatric AR patients. Consistent with our results, a study by Wei et al. [28] reported that MKS significantly reduced IL-4 and EOS levels in children with cough-variant asthma.

Additionally, our results suggest that MKS combined with LEVO nasal spray significantly enhances quality of life in pediatric AR patients. This therapeutic advantage is likely attributable to the synergistic effects of the combination therapy, which effectively controls clinical symptoms, improves nasal conditions, and suppresses systemic inflammation and disease progression. Consequently, this comprehensive approach facilitates recovery and leads to substantial improvements in patient quality of life. Supporting these findings, a study by Kim et al. [29] demonstrated that MKS combined with levocetirizine effectively managed daytime nasal congestion, rhinorrhea, and nocturnal nasal obstruction in pediatric AR patients, while also exhibiting lower adverse event rates and higher overall satisfaction. Moreover, Guo et al. [30] reported that combining MKS with

budesonide significantly improved pulmonary function in children with concomitant AR and asthma. This regimen not only alleviated symptoms of both conditions but also contributed to IgE reduction and a lower EOS percentage, further validating our findings.

Notably, both univariate and multivariate analyses confirmed that pediatric AR patients exposed to passive secondhand smoke and those with elevated EOS levels faced a significantly higher risk of treatment failure.

Despite these promising findings, this study has several limitations. The study did not extensively investigate potential factors affecting patient safety. Further analyses focusing on safety parameters would provide more specific and clinically relevant insights. As a single-center study, there may be inherent selection and information biases. Future multicenter studies are needed to enhance the generalizability of these findings. What's more, the precise therapeutic mechanisms underlying the combination therapy of MKS and LEVO nasal spray in pediatric AR were not thoroughly explored. Additional basic research is required to elucidate these mechanisms.

Future research efforts should address these limitations to further advance our understanding of this treatment approach.

In conclusion, the combination of MKS and LEVO nasal spray provides superior clinical efficacy with a favorable safety profile in pediatric AR patients. This regimen effectively alleviates rhinorrhea, sneezing, nasal congestion, and nasal pruritus, improves nasal cavity conditions, modulates serum inflammatory responses, and restores serum biochemical indices, ultimately enhancing the quality of life.

However, it is important to recognize that pediatric AR patients with passive secondhand smoke exposure and elevated EOS levels face a significantly higher risk of treatment failure. These findings highlight the need for personalized treatment strategies and targeted interventions to optimize therapeutic outcomes in high-risk pediatric AR populations.

Disclosure of conflict of interest

None.

Address correspondence to: Dehong Mao, Department of Otolaryngology, Yongchuan Hospital of Traditional Chinese Medicine, Chengdu University of Traditional Chinese Medicine, Chongqing 402160, China. Tel: +86-023-49826120; E-mail: dehongmao1963@163.com

References

[1] Hu Y, Luo H, Li J, Zhang R, Fu L, Ren Q, Chen Y, Huang X, Zhou Z, Yuan H, Tian L and Wang X. Immunofluorescent labeling in nasal mucosa tissue sections of allergic rhinitis rats via multicolor immunoassay. J Vis Exp 2023.

[2] Bernstein JA, Bernstein JS, Makol R and Ward S. Allergic rhinitis: a review. JAMA 2024; 331: 866-877.

[3] Zhang M, Ni JZ and Cheng L. Safety of intranasal corticosteroids for allergic rhinitis in children. Expert Opin Drug Saf 2022; 21: 931-938.

[4] Licari A, Magri P, De Silvestri A, Giannetti A, Indolfi C, Mori F, Marseglia GL and Peroni D. Epidemiology of allergic rhinitis in children: a systematic review and meta-analysis. J Allergy Clin Immunol Pract 2023; 11: 2547-2556.

[5] Eremija J and Carr TF. Immunotherapy for asthma. Semin Respir Crit Care Med 2022; 43: 709-719.

[6] Couroux P, Grosse N, Salapatek AM, Goyal Y, Pfaar O and Hohenfeld IP. Barrier-forming, drug-free nasal spray reduces allergic symptoms induced by house dust mite allergen. Clin Transl Allergy 2023; 13: e12277.

[7] Bousquet J, Anto JM, Bachert C, Baiardini I, Bosnic-Anticevich S, Walter Canonica G, Melen E, Palomares O, Scadding GK, Togias A and Toppila-Salmi S. Allergic rhinitis. Nat Rev Dis Primers 2020; 6: 95.

[8] Tosca MA, Trincianti C, Naso M, Nosratian V and Ciprandi G. Treatment of allergic rhinitis in clinical practice. Curr Pediatr Rev 2024; 20: 271-277.

[9] Mandhane SN, Shah JH and Thennati R. Allergic rhinitis: an update on disease, present treatments and future prospects. Int Immunopharmacol 2011; 11: 1646-1662.

[10] Han D, Chen L, Cheng L, Liu S, Fu Z, Zhang W, Wang C, Xi L and Zhang L; Chinese Allergic Rhinitis Collaborative Research Group (C2AR2G). A multicenter randomized double-blind 2-week comparison study of azelastine nasal spray 0.1% versus levocabastine nasal spray 0.05% in patients with moderate-to-severe allergic rhinitis. ORL J Otorhinolaryngol Relat Spec 2011; 73: 260-265.

[11] Zhu XH, Tu JW and Dai JH. Clinical effect of fluticasone propionate, montelukast sodium

and ketotifen in treatment of cough variant asthma in children. Zhongguo Dang Dai Er Ke Za Zhi 2019; 21: 393-398.
[12] Mao X and Zhao W. Efficacy of montelukast combined with sublingual immunotherapy in the treatment of children with obstructive sleep apnea hypopnea syndrome complicated with allergic rhinitis. Pak J Med Sci 2023; 39: 1350-1354.
[13] Wang H, Ji Q, Liao C and Tian L. A systematic review and meta-analysis of loratadine combined with montelukast for the treatment of allergic rhinitis. Front Pharmacol 2023; 14: 1287320.
[14] Shao M, Sun J and Zheng Q. Efficacy and safety of montelukast-levocetirizine combination therapy in combined allergic rhinitis and asthma syndrome: a systematic review and meta-analysis. J Asthma 2025; 62: 376-385.
[15] Siddiqui ZA, Walker A, Pirwani MM, Tahiri M and Syed I. Allergic rhinitis: diagnosis and management. Br J Hosp Med (Lond) 2022; 83: 1-9.
[16] He M, Qin W, Qin Z and Zhao C. Acupuncture for allergic rhinitis: a systematic review and meta-analysis. Eur J Med Res 2022; 27: 58.
[17] Alamri RA, Aljabri GH, Tahlawi R and Aljabri HA. Immunotherapy in the treatment of allergic rhinitis in children. Cureus 2022; 14: e32464.
[18] Yao X, Liu Y, Jiao H, Ma W and Chen M. Association of LOX gene G473A polymorphism with the occurrence of allergic rhinitis and efficacy of montelukast sodium in children. Cell Cycle 2023; 22: 2280-2287.
[19] Phan H, Moeller ML and Nahata MC. Treatment of allergic rhinitis in infants and children: efficacy and safety of second-generation antihistamines and the leukotriene receptor antagonist montelukast. Drugs 2009; 69: 2541-2576.
[20] Micheletto C, Tognella S, Visconti M, Pomari C, Trevisan F and Dal Negro RW. Montelukast 10 mg improves nasal function and nasal response to aspirin in ASA-sensitive asthmatics: a controlled study vs placebo. Allergy 2004; 59: 289-294.
[21] Yang C, Shangguan C, Cai C, Xu J and Qian X. LncRNA HCP5 participates in the tregs functions in allergic rhinitis and drives airway mucosal inflammatory response in the nasal epithelial cells. Inflammation 2022; 45: 1281-1297.
[22] Vlaykov AN, Tacheva TT, Vlaykova TI and Stoyanov VK. Serum and local IL-4, IL-5, IL-13 and immunoglobulin E in allergic rhinitis. Postepy Dermatol Alergol 2020; 37: 719-724.
[23] Zhu F, Sun K, Yu L, Sun S, Wan Y and Shi L. Tissue cytokine adenoid experssion in hypertrophic adenoid gland in children with allergic rhinitis. J Coll Physicians Surg Pak 2021; 31: 903-909.
[24] Boonpiyathad T, Tantilipikorn P, Ruxrungtham K, Pradubpongsa P, Mitthamsiri W, Piedvache A, Thantiworasit P, Sirivichayakul S, Jacquet A, Suratannon N, Chatchatee P, Morisaki N, Saito H, Sangasapaviriya A, Matsumoto K and Morita H. IL-10-producing innate lymphoid cells increased in patients with house dust mite allergic rhinitis following immunotherapy. J Allergy Clin Immunol 2021; 147: 1507-1510 e1508.
[25] Wang J, Yang Y, Cao J, Song X, Guo J, Yu P, Liu Z, Zhang W, Liu X, Zhang Y and Song X. Total serum immunoglobulin E (IgE) as an effective predictor for identifying allergic asthma in childhood asthma. Allergy Asthma Proc 2023; 44: 252-257.
[26] Liu B, Huang X, Xia L, Wang D, Mu D and Tian L. Effects of Yupingfeng nasal drops on serum cytokines, histopathology and eosinophil cationic protein in nasal mucosa of rats with allergic rhinitis. Pak J Pharm Sci 2021; 34: 1351-1358.
[27] Yoon H, Kwak IY, Kim K and Min HJ. Chronic rhinosinusitis with nasal polyps does not affect the association between the nasal provocation test and serum allergen-specific immunoglobulin E levels. J Rhinol 2024; 31: 29-36.
[28] Wei H, Li W, Jiang Z, Xi X and Qi G. Clinical efficacy of montelukast sodium combined with budesonide or combined with loratadine in treating children with cough variant asthma and influence on inflammatory factors in the serum. Exp Ther Med 2019; 18: 411-417.
[29] Kim CK, Hwang Y, Song DJ, Yu J, Sohn MH, Park YM, Lim DH, Ahn K and Rha YH. Efficacy and safety of montelukast+levocetirizine combination therapy compared to montelukast monotherapy for allergic rhinitis in children. Allergy Asthma Immunol Res 2024; 16: 652-667.
[30] Guo S and Cao C. Effects of montelukast sodium combined with budesonide on pulmonary function, serum IgE levels, and EOS percentage in children with comorbid allergic rhinitis and asthma. Am J Transl Res 2023; 15: 6823-6831.